directed to inhibit expression of both the GAD_{65}, and GAD_{67} isoforms are used. Support for new claims 34-37 is found throughout the specification and claims as originally filed. No new matter has been added.

Claims 23 and 28 have been amended to more clearly recite that the oligonucleotides used in the claimed methods are effective to inhibit expression of GAD_{65}, or GAD_{67}. As amended, the claims are limited to those embodiments in which the oligonucleotide is functional. Support for the amendment is found throughout the specification and claims as originally filed. No new matter has been added.

Claim 30 has been amended to incorporate all of the limitations of claim 29 from which it depended. Support for the amendments is found throughout the specification and claims as originally filed. No new matter has been added.

Preliminary Remarks

As a preliminary matter, Applicants acknowledge that that the subject matter in claims 1-4, 9-12 and 23-33 has been deemed free of the prior art, and that claims 1-4 and 9-12 are allowable. Applicants present this amendment to place the remaining claims in allowable form.

Specification

Objections were made to the specification for the inclusion of hyperlinked text on pages 8 and 9. The objected to text has been deleted and the objection is obviated.

Rejections under 35 USC §112

Claims 23-29 and 31-33 stand rejected under 35 U.S.C. § 112, first paragraph, because it is asserted that the specification fails to provide an enabling disclosure "for administration of any of (*sic*) antisense to GAD as instantly claimed." (Page 3 of Official Action). Applicants respectfully disagree.

The reason provided in support of the rejection is that the teachings in the specification do "not correlate to the design and use of any other individual antisense oligonucletide." (Page 3-4 of Official Action). It is asserted that the specification is not enabled for antisense to any GAD gene.

The claims have been amended to more specifically recite the scope of the claims in an effort to more clearly set forth the invention as enabled. Amended claims 23 and 28 recite that the

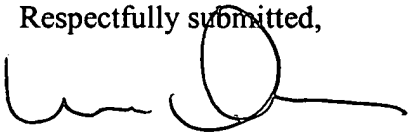
glutamic acid decarboxylase is GAD_{65} or GAD_{67} and that the antisense oligonucleotide inhibits expression of GAD_{65} or GAD_{67} mRNA. One skilled in the art would be able to practice the claimed invention without being required to perform undue experimentation.

Those skilled in the art could routinely produce, test and identify the various antisense oligonucleotides within the scope of the invention without undue experimentation. There is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation in order to make and use the claimed invention. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

In view of the foregoing, Applicant respectfully submits that all pending claims are in condition for allowance. An early notice of the same is earnestly solicited. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The following paragraph beginning on page 8, line 27 has been amended as follows:

These sequences were obtained by searching Genbank for the appropriate gene name. These sequences were analyzed using an open reading frame finder program at the National Center for Biotechnology Information [World Wide Web site (http://www.ncbi.nlm.nih.gov/cgi-bin/gorf/orfig)] and is publicly available through the Internet at the world wide web at, for example, ncbi.nlm.nih.gov/cgi-bin/gorf/orfig. The initiation of translation site was found and a 21 base antisense molecule complementary to the region spanning 8 bases 5' to 13 bases 3' (-8 to +13) to the initiation triplet was selected. These 21 base oligonucleotides were analyzed for cross reactivity with other genes using the NCBI BLAST server [(http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/)] and is publicly available through the Internet at the world wide web at, for example, ncbi.nlm.nih.gov/cgi-bin/BLAST/.

In the Claims:

Claims 27 and 33 have been canceled. Claims 34-37 have been added and claims 23, 28 and 30 have been amended as follows:

23. (Amended) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of an antisense oligonucleotide effective to inhibit translation of [directed to] glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase wherein said glutamic acid decarboxylase is GAD_{65}, or GAD_{67}.

28. (Amended) A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide effective to inhibit translation of [directed to]

glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula wherein said glutamic acid decarboxylase is GAD_{65}, or GAD_{67}.

30. (Amended) A [The] method of [claim 29] downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula, wherein said antisense oligonucleotide is directed to the initiation codon of glutamic acid decarboxylase mRNA, and said antisense oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5.